

**CLEAN COPY OF PENDING CLAIMS (As of Feb. 27, 2003)**

2. A recombinant allergen according to claim 48, obtainable by

a) identifying amino acid residues in a naturally occurring allergen

originating from one of the taxonomic orders *Fagales*, *Hymenoptera* or *Dermatophagoides* which are conserved with more than 70% identity in all of the known homologous proteins within the taxonomic order from which said naturally occurring allergen originates;

b) defining at least one patch of conserved amino acid residues being

coherently connected over at least  $400 \text{ \AA}^2$  of the surface of the three-dimensional structure of the naturally occurring allergen molecule as defined by having a solvent accessibility of at least 20%, said at least one patch comprising at least one B cell epitope; and

c) substituting at least one amino acid residue in said at least one patch with

another non-conservative amino acid, wherein the  $\alpha$ -carbon backbone tertiary structure of the allergen molecule is conserved.

3. A recombinant allergen according to claim 48, wherein the specific IgE binding to the mutant allergen is reduced by at least 5%, preferably at least 10%.

5. A recombinant allergen according to claim 2, wherein said at least one patch consists of at least 15 amino acid residues.

6. A recombinant allergen according to claim 2, wherein the amino acid residues of said at least one patch are ranked with respect to solvent accessibility, and one or more amino acids among the more solvent accessible ones are substituted.

7. A recombinant allergen according to claim 6, wherein one or more amino acid residues of said at least one patch having a solvent accessibility of 20-80% are substituted.

8. A recombinant allergen according to claim 2, wherein 1-5 amino acid residues per 400Å<sup>2</sup> in said at least one patch are substituted.

9. A recombinant allergen according to claim 2, wherein the substitution of one or more amino acid residues in said B cell epitope or said at least one patch is carried out by site-directed mutagenesis.

12. A recombinant allergen according to claim 48, wherein the allergen is derived from a pollen allergen originating from the taxonomic order of *Fagales*.

13. A recombinant allergen according to claim 12, wherein the allergen is derived from *Bet v 1*.

14. A recombinant allergen according to claim 13, wherein at least one amino acid residue of said B cell epitope or said at least one patch is substituted.

19. A recombinant allergen according to claim 48, wherein the allergen is derived from a mite allergen originating from *Dermatophagoides*.

24. A recombinant allergen according to claim 48 wherein the allergen is derived from a venom allergen originating from the taxonomic order of *Hymenoptera*.

25. A recombinant allergen according to claim 24 wherein the allergen is derived from a venom allergen from the taxonomic order of *Vespidae*, *Apidae* and *Formicoidae*.

26. A recombinant allergen according to claim 24, wherein the allergen is derived from *Ves v 5*.

28. A recombinant allergen according to claim 26, wherein said allergen has one or more amino acid substitution is selected from the group consisting of

- (i) Lys at position 72 of SEQ ID NO: 39 substituted with Ala; and
- (ii) Tyr at position 96 of SEQ ID NO: 39 substituted with Ala.

32. A recombinant allergen according to claim 48 for use as a pharmaceutical.

33. A pharmaceutical composition, comprising a recombinant allergen according to claim 48, optionally in combination with a pharmaceutically acceptable carrier and/or excipient, and optionally an adjuvant.

34. A pharmaceutical composition according to claim 33, in the form of a vaccine against allergic reactions elicited by a naturally occurring allergen in patients suffering from allergy.

47. A pharmaceutical composition obtainable by the process according to claim 33.

48. A recombinant mutant allergen derived from a naturally occurring allergen originating from one of the taxonomic orders *Fagales*, *Hymenoptera* or *Dermatophagoides* in which at least one surface-exposed, amino acid residue of a B cell epitope at a position which is conserved in the amino acid sequences of homologous proteins within the taxonomic order from which the naturally occurring allergen originates, is substituted with an amino acid residue which is not conserved in the same position in the amino acid sequences of homologous proteins within the taxonomic order from which the naturally occurring allergen originates, wherein the  $\alpha$ -carbon

backbone tertiary structure of the recombinant allergen is conserved as compared with the  $\alpha$ -carbon backbone tertiary structure of the naturally occurring allergen, and specific IgE binding to the mutant allergen is reduced compared to the IgE binding to the naturally occurring allergen.

49. A recombinant allergen according to claim 48, wherein the average root mean square deviation of the atomic coordinates comparing the  $\alpha$ -carbon backbone tertiary structures of the mutant and the naturally occurring allergen molecules is below 2Å.

50. A recombinant allergen according to claim 14 wherein said allergen has one or more amino acid substitutions selected from the group consisting of:

- (i) Thr at position 10 of SEQ ID NO: 37 substituted with Pro;
- (ii) Asp at position 25 of SEQ ID NO: 37 substituted with Gly;
- (iii) Asn at position 28 of SEQ ID NO: 37 substituted with Thr, and Lys at position 32 of SEQ ID NO: 37 substituted with Gln;
- (iv) Glu at position 45 of SEQ ID NO: 37 substituted with Ser;
- (v) Asn at position 47 of SEQ ID NO: 37 substituted with Ser;
- (vi) Lys at position 55 of SEQ ID NO: 37 substituted with Asn;
- (vii) Thr at position 77 of SEQ ID NO: 37 substituted with Ala;
- (viii) Pro at position 108 of SEQ ID NO: 37 substituted with Gly; and
- (ix) Asn at position 28 of SEQ ID NO: 37 substituted with Thr, Lys at position 32 of SEQ ID NO: 37 substituted with Gln, Glu at position 45 of SEQ ID NO: 37 substituted with Ser and Pro at position 108 of SEQ ID NO: 37 substituted with Gly.

51. A recombinant allergen according to claim 5, wherein said at least one patch consists of 15-25 amino acid residues.